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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	
JONATHAN S. STAMLER	Group Art Unit: 1654
Patent Application No. 09/757,610	Examiner: R.R. Teller
Filed: January 11, 2001	Confirmation No. 8014
For: INHIBITING GS-FDH TO MODULATE NO BIOACTIVITY	

REPLY BRIEF ON APPEAL (In Triplicate)

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in reply to the Examiner's Answer of March 8, 2004.

The Reply Brief is taking the position that the non-enablement rejection is a scope of enablement rejection. The undersigned contests this because the basis of the rejection is one of operativity, namely that the administration "does not reasonably provide enablement for killing or reducing the growth of pathologically proliferating mammalian cells *in vivo*" and the PTO has not met the PTO guidelines for this. See MPEP §2107.

But even assuming that the issue is scope of enablement (which it is not), the PTO's position is defective. For scope of enablement rejections, the burden is on the PTO to support by evidence or reasoning its doubts on enablement. See In re Dinh-Nguyen, 181 U.S.P.Q. 46 (CCPA 1974); In re Bowen, 181 U.S.P.Q. 48 (CCPA 1974); In Re Ambruster, 185 U.S.P.Q. 152 (CCPA 1975); and Ex parte Reese, 40 U.S.P.Q. 2nd 1221 (Bd. App. 1996).

The only evidence relied on by the PTO is Dermer, Biotechnology 12, 320 (3/94) which has been reinstated in response to appellant's position that no evidence was relied on. The only reasoning of the PTO is based on Dermer or is inappropriately based on *ipse dixit.*

The evidentiary value of Dermer was overcome by applicant's position set forth in the response of June 9, 2003; relevant portions are set forth below:

> Dermer is submitted to be defective for the purpose on which it is relied.
>
> Firstly, this is because there is a Commissioner's Decision which indicates that reliance on Dermer would be misplaced. In this regard, see In re Hozumi, 226 U.S.P.Q. 353 (Comm Dec. 1985). Hozumi holds that cell line data for human myelocytic leukemia cells HL-60 is sufficient for *in vivo* treatment claims in respect to leukemia and suggests that cell line data for solid tumor cell lines would be sufficient for claims in respect to treatment of solid tumors. The instant case meets the Commissioner's Decision test for lymphoma/leukemia treatment and for solid tumor treatment. Background Example 1 at pages 32 and 33 of the application as filed, provides data on a human acute monocytic leukemia cell line (THP-1) as well as on the solid tumor cell lines HeLa (derived from adenocarcinoma of the cervix) and A549 (derived from liver carcinomatous tissue). Thus Hozumi indicates there is sufficient data here for *in vivo* utility. Hozumi has not been withdrawn or reversed despite Dermer (1994). Use of human cancer cell lines is still standard operating procedure, for cancer research. The PTO is still granting patents where the only evidence of *in vivo* anti-cancer utility is cell line data . See Dannenberg et al U.S. Patent No. 6,291,490.
>
> Secondly, Dermer is submitted to be defective because Dermer is making a general assertion. Rather the PTO needs to cast doubt on the specific usefulness in this case. For example, the PTO needs to show that the specific cell lines used here do not mimic the human body. Or the PTO needs to cast doubt on the specific usefulness of some specific treating agent set forth in the application. See In re Brana, 34 U.S.P.Q. 2d 1436, 1441 (Fed. Cir. 1995).
>
> Thirdly, Dermer is submitted to be defective because cells that Dermer mentions are much different from the cell lines tested in the instant patent application. Dermer discusses 3T3 cells. 3T3 cells are embryonic fibroblast cell lines derived from Swiss mice, used for transfection studies with a DNA virus. This is much different from the case here where cell lines obtained from human cancer cells, and representing actual human leukemia/lymphoma and tumors, are used to determine the presence of an enzyme activity to understand a mechanism for *in vivo* treatment of cancer.

Fourthly, the rejection is defective because the action has not shown that the Dermer thesis is generally accepted by the scientific community. The Dermer citation is one researcher's opinion and is clearly controversial. Consider the following statement by a review of Dermer's book which presents the same thesis.

> The book does have its limitations. Dermer apparently wrote this partly to inform the public, partly to level some scores in his profession. He is less successful at presenting another model for research than in explaining the shortcoming of current cellular research. He suggests animal research but fails to review the logical results of that theory. Instead of testing cells in the laboratory, will we experiment on millions of beagles? Ultimately the book is limited because the author fails to thoroughly explore his own theories.

Dermer's thesis is recognized as limited and therefore insufficient to support the rejection.

None of these defects in Dermer pointed out above have been responded to by the PTO. It therefore should be found that these positions are uncontested.

We turn now to the specific responses to appellant's five positions set forth as required under 37 C.F.R. 1.192 (c)(8)(i) at pages 8-11 of its brief.

The first error pointed out by appellant in its brief is that there is no enablement issue because the application teaches how to use. The PTO's rejoinder is that more is necessary for scope of enablement rejections. This is treated above.

The second error pointed out by appellant in its brief is that the rejection is contrary to the presumptive enablement provided by U.S. Patent No. 6,057,367. The reply to this in the Examiner's Answer is that U.S. Patent No. 6,057,367 does not use d-glutathione. The rejoinder to this is that the PTO has conceded enablement with respect to treating agent.

The third error pointed out by appellant in its brief is that the standard of requiring the clinical results to be shown to invariably occur, is defective. Appellant's position is that this

standard cannot be appropriate because no medical treatment meets this standard (regardless of case, some patients do not benefit). The PTO has not met this position.

The fourth error pointed out by appellant in its brief is that any requirement for providing disclosure about pitfalls is not appropriate because the evidence relied on by the PTO does not teach there are any pitfalls in this case. The Examiner's Answer relies on Dermer. This is submitted to be a defective position. Dermer is not specific enough to the facts of the instant case, to indicate pitfalls for the instant case.

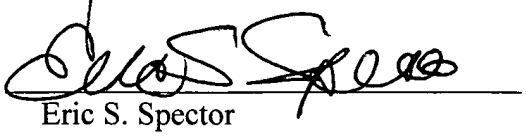
The fifth error pointed out by appellant in its brief is that the rejection is based on no evidence. Now there is reliance only on Dermer. Dermer is rebutted above.

In addition, appellant in its brief at pages 11 and 12, has taken the position that Claims 9, 12 and 13 are patentable for additional reasons. The Examiner's Answer in response to the position on Claim 9 says there are no working examples on this. It is submitted that there need not be working examples, but the PTO's position is factually in error in that Examples XV and XVI (page 40) are pertinent.

The Examiner's Answer does not seem to respond to appellant's additional positions on Claims 12 and 13.

Reversal of the rejections and allowance of Claims 8-14 is requested.

Respectfully submitted,

By: 

Eric S. Spector
Reg. No. 22,495

BACON & THOMAS PLLC
Fourth Floor
625 Slaters Lane
Alexandria, Virginia 22314-1176
703-683-0500

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